Neonatal pertussis: life-threatening event and outbreak prevention in the NICU

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Title figure:
Bordetella pertussis: 3D computer-generated artistic recreation based on scanning electron microscopic images (source: CDC / Sarah Bailey Cutchin / Illustrator: Meredith Newlove).

CASE REPORT

A 22-day-old male infant (corrected gestational age of 37 5/7 weeks) was brought to the hospital because of numerous apneic episodes. He had been born prematurely at 34 4/7 weeks of gestation due to amniotic infection syndrome. His birthweight had been 2220 g (P25 – 50). Pregnancy, vaginal delivery and adaptation had been uncomplicated. The infant received phototherapy for neonatal jaundice from day of life (DOL) 5 to 7.

The parents described recurrent episodes of aspiration since DOL 17, and a one-day history of poor feeding. On admission, the infant was sleepy, inactive, and showed inappropriate response to handling. Numerous apneic episodes were noted. The clinical examination was remarkable for jaundice, prolonged capillary refill time (3 – 4 seconds), dry mucosal membranes and a sunken fontanel.

Blood cultures were obtained, and empiric treatment with amoxicillin and gentamicin was started to treat possible bacterial sepsis. Due to poor respiratory effort and recurrence of apnea, the boy had to be intubated.

The initial working hypothesis was late onset sepsis or a respiratory viral infection, such as respiratory syncytial virus (RSV). Other differential diagnoses were also considered: metabolic disease (prolonged jaundice), convulsions or energy deficiency as a result of poor feeding.

Except for leukocytosis (leukocyte count 21.84 G/l, neutrophils 7.80 G/l, lymphocytes 12.19 G/l) and a previously known slight increase of liver function tests (bilirubin, LDH and GGT), laboratory results (including C-reactive protein, interleukin-6, electrolytes, ammonia and renal function tests) were normal. A chest radiograph showed bilateral peribronchial consolidations suggestive of aspiration pneumonia (Fig. 1). Echocardiography and cranial ultrasound examination were also normal. Unblinding of the newborn screening test showed normal results.

Fig. 1

Chest X-ray following intubation showing bilateral peribronchial consolidations.

One day after admission, a tracheal aspirate sample was reported to be positive for Bordetella pertussis. Antibiotic therapy was therefore changed to intravenous azithromycin 10 mg/kg 24-hourly for 5 days (1). Droplet isolation was added to the previously ordered contact isolation.

The infant's mother and sister reported a history of coryza and cough over the past 3 weeks. The vaccination status of the 4-year-old sister was up to date. The infant's father had received pertussis vaccination 6 years ago; the mother's last booster had occurred 10 years ago. She had not been immunized during pregnancy. The parents and sister received post-exposure prophylaxis (PEP). The mother's nasal swab and blood tests (including blood count, C-reactive protein, electrolytes, coagulation tests, liver and renal function) were unremarkable.

In order to protect the other newborns in the ward, all staff members who had had contact with the patient prior to droplet isolation precautions were required to take PEP with oral azithromycin for 5 days and to wear a surgical mask during the same time period (regardless of their vaccination status). The team members who refused PEP were asked to wear a surgical mask for 21 days. Because of the high risk for the premature babies in our NICU, the baby with pertussis was transferred to a pediatric intensive care unit (PICU). The infant required respiratory support for

5 days (invasive mechanical ventilation for 2 days, CPAP for 1 day and low flow for another 2 days) and received caffeine therapy for 12 days. He could be discharged after a 20-day hospitalization.

DISCUSSION

Despite a widespread vaccination program, pertussis continues to be a common infection in the pediatric and adult population worldwide. In 2018, the World Health Organization (WHO) reported 151'074 cases of pertussis despite an estimated global diphtheria-tetanus-pertussis (DTP) vaccine coverage with three doses (2) of 86%.

Pertussis is a highly contagious acute respiratory disease that is often underdiagnosed. The majority of cases (86 – 95%) is caused by Bordetella pertussis with the remaining cases being caused by Bordetella parapertussis (3 – 5). Bordetella species are gram-negative, aerobic, encapsulated coccobacilli. Transmission occurs via aerosolized respiratory droplets. After an incubation period of 4 – 21 days (typically 7 – 10 days), symptoms develop and typically last for 6 to 12 weeks (sometimes longer).

Classical pertussis, as it is seen in unvaccinated children, is characterized by three stages: stadium catarrhale (similar to a viral upper respiratory infection with mild cough and coryza), stadium convulsivum (coughing spells of increasing severity with or without post tussive vomiting), and stadium decrementi (decreasing severity of the clinical symptoms). In infants younger than 3 months, the catarrhal stage can be shorter than in older children and can remain unrecognized, whereas stadium convulsivum and decrementi are usually prolonged (3, 4, 6).

Apart from coughing, pertussis in this age group often causes apnoea, which can be the first symptom of the disease. 18% of infected infants < 12 months of age require hospitalization, with apnoea occurring in 61% and pneumonia occurring in 23% of these cases. Many require supplemental oxygen, and some need mechanical ventilation because of acute respiratory distress syndrome (with or without pulmonary hypertension) or apnoea. Seizures (1%) are also a known complication (7). Another well-known finding is severe hyperviscosity of the blood due to the pathognomonic hyperleukocytosis, which can lead to death in young infants (8).

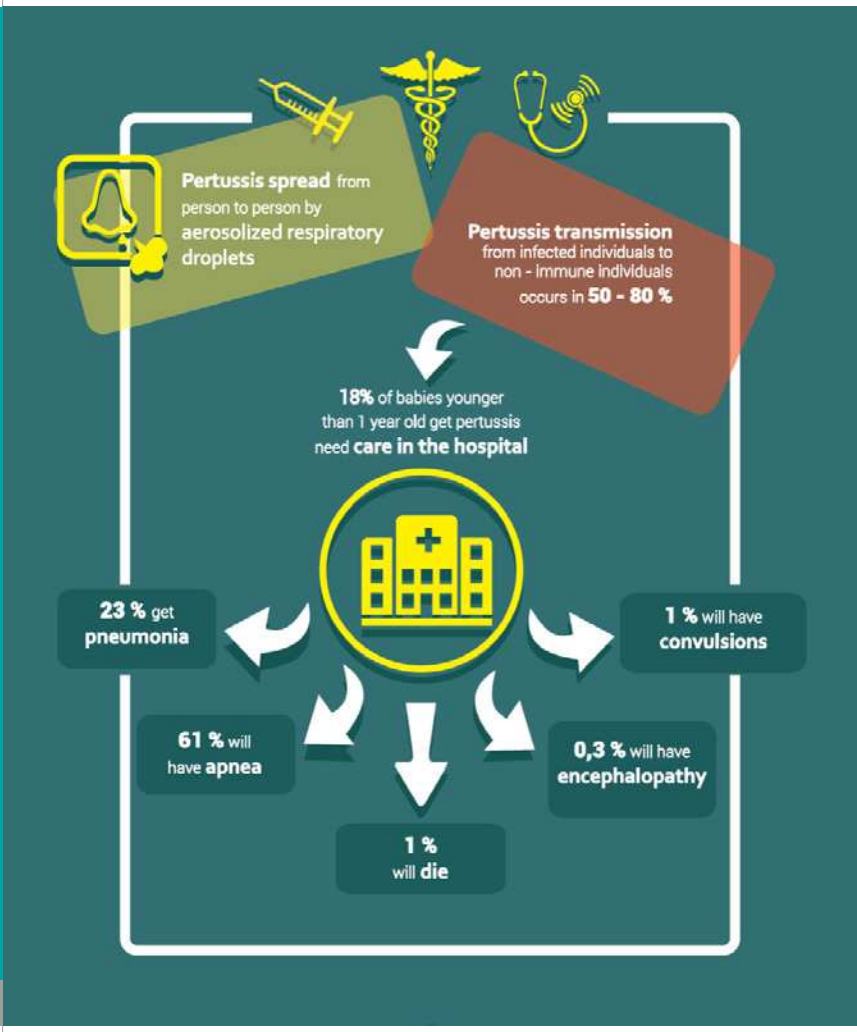

Fig. 2

Pertussis: transmission and complications (graphic designer: Chiara Benetton) (4,7).

The severity of the disease is inversely related to the age of the patient. Neonates and toddlers have higher morbidity – as described above – and mortality rates (3, 9). Apart from the patient's age, the clinical manifestations are influenced by the immunization status and – in newborns – the amount of transplacentally acquired antibodies. The overall lethality of pertussis infection is estimated to be 0,05 per 1'000 cases. The mortality rate is four times higher in children from birth to 5 years of age (0,2 deaths per 1'000 cases) with infants less than 3 months of age being at highest risk with about 10 deaths per 1'000 cases (4).

The burden of the disease calls for preventative measures against pertussis in infants, especially in newborns. Several strategies have been proposed to protect neonates. Maternal vaccination during pregnancy is the most effective strategy to date. It leads to transplacental transfer of IgG antibodies to the fetus. After birth, the neonate receives additional antibodies, especially of the IgA isotype, via breastmilk. These antibodies protect the neonate against infections in the first months of life when the immune system is still immature and active immunity has not yet been acquired (10, 11). Additionally, efforts should be made to achieve a high immunization rate in the general population, especially in people having contact with young children and prospective parents (cocoon strategy) (10, 12).

Individuals with suspected or proven pertussis should avoid contact with infants and women in late pregnancy, especially with those who have not been immunized, until five days of antibiotic treatment have been completed. Untreated patients should avoid contact with high-risk individuals for the full infectious period (1, 6). For hospitalized infected patients, droplet and contact isolation are mandatory to reduce the spread of the disease (6). In case of a pertussis outbreak in the hospital, under-vaccinated persons with contact to pertussis cases should be identified and a pertussis-containing vaccine should be administered. Admittedly, such vaccination might not prevent illness in a person who has already been infected with Bordetella pertussis. Generally, PEP is recommended depending on age and vaccination status. More detailed information has been published by the Swiss Federal Office of Public Health (BAG) (13). PEP is always recommended for under-vaccinated exposed healthcare workers who have contact with high-risk patients (1, 6).

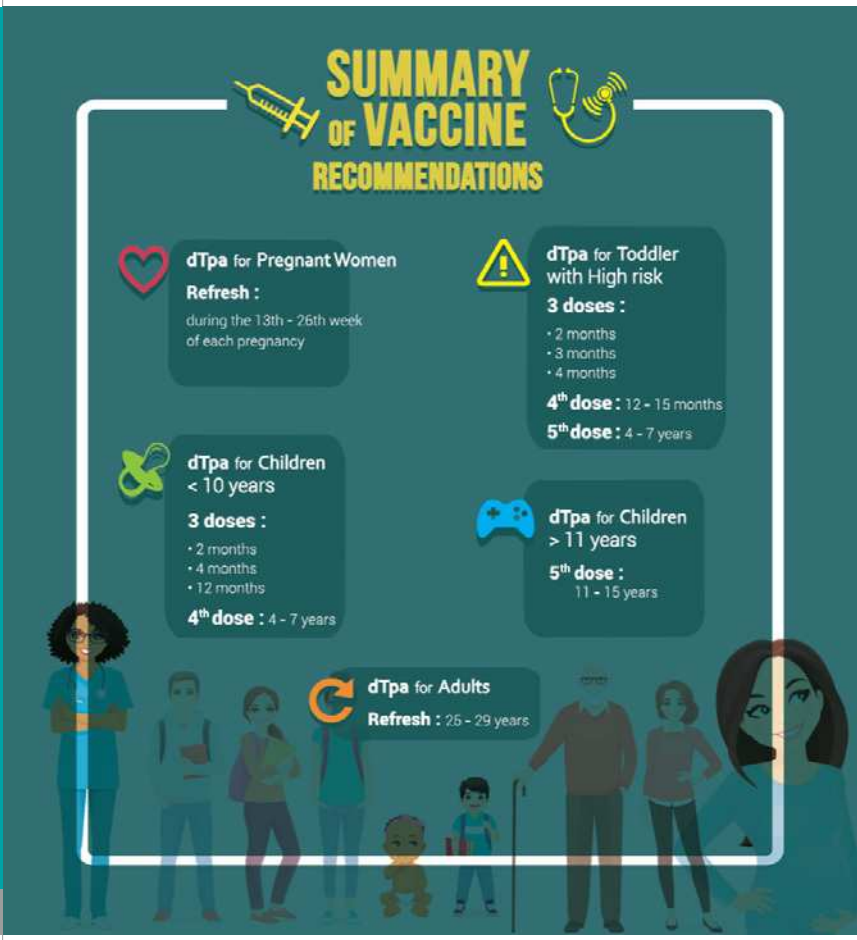

Fig. 3

Pertussis: summary of vaccination recommendations (toddler with high risk: infant attending childcare facilities, very low gestational age infants, all infants during pertussis outbreaks) (graphic designer: Chiara Benetton) (4).

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